13/D
B. Wehl
2/22/01

RESPONSE UNDER 37 CFR §1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1655

CERTIFICATE OF MAILING			
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.			
Typed or Printed Name	Donna Macedo		
Signature	D. Macedo	**Date**	2/9/01

AMENDMENT UNDER 37 C.F.R. §1.116 EXPEDITED PROCEDURE EXAMINING GROUP 1655

Address to:
Box AF
Commissioner for Patents
Washington, D.C. 20231

Attorney Docket	10981620-1
First Named Inventor	Delenstarr
Application Number	09/398,399
Filing Date	September 17, 1999
Group Art Unit	1655
Examiner Name	B. Sisson
Title	Techniques for Assessing Non-Specific Binding of Nucleic Acids to Surfaces

Sir:

This amendment is responsive to the Final Office Action dated November 7, 2000 for which a three-month period for response was given making this response due on or before February 7, 2001. In view of the amendments to the claims and the remarks put forth below, reconsideration and allowance are respectfully requested.

DO NOT ENTER
2/23/01
B.S.

AMENDMENTS

IN THE CLAIMS:

Please amend claims 10, 15, 21, 24, 30, 34, 40 43, 44 and 49 as shown below.

10. (Amended) A hybridization assay, said assay comprising:

(a) providing a sample of labeled target nucleic acids, wherein said sample comprises a labeled positive control target nucleic acid;

(b) contacting said sample under [stringent] hybridization conditions that require a target nucleic acid of 14 nucleotides in length to have at least 70% sequence identity with a probe in order to hybridize to said probe with a collection of substrate bound nucleic acid features comprising:

(i) hybridization probes that include a positive control probe, and

(ii) background features

wherein said substrate bound nucleic acid features are present on said substrate in a spatially defined and a physically addressable manner;

(c) removing unhybridized target nucleic acids from said substrate;

(d) detecting an observed signal for each resultant detectable hybridization probe feature of said substrate;

(e) determining a background signal by detecting a signal for each background feature and averaging said background feature signals;

(f) subtracting the background signal from the observed signal for each hybridization probe feature.

15. (Amended) The assay of claim 10, wherein the background features comprise probes selected from the group consisting of empirically observed inactive probes, probes forming [stable] intramolecular structures, short probes of 5 to 25 nt in length, reverse polarity nucleotide analogs, abasic phosphodiesters or modified nucleotidic units.

21. (Amended) A method for estimating background noise in a nucleic acid hybridization assay, said method comprising:

(a) providing a sample of labeled target nucleic acids, wherein said sample comprises a labeled positive control target nucleic acid;

(b) contacting said sample under [stringent] hybridization conditions that require a target nucleic acid of 14 nucleotides in length to have at least 70% sequence identity with a probe in order to hybridize to said probe with a collection of substrate bound nucleic acid features comprising:

(i) hybridization probes that include a positive control probe, and

(ii) background features

wherein said substrate bound nucleic acid features are present on said substrate in a spatially defined and a physically addressable manner;

(c) removing unhybridized target nucleic acids from said substrate;

(d) determining a background signal by detecting a signal for each background feature and

averaging said background feature signals.

24. (Amended) The method of claim 21, wherein the background features comprise probes selected from the group consisting of empirically observed inactive probes, probes forming [stable] intramolecular structures, short probes of from 5 to 25 nt in length, reverse polarity nucleotide analogs, abasic phosphodiesters or modified nucleotidic units.

30. (Amended) A method of validating a test-background feature, said method comprising:

(a) providing a sample of labeled target nucleic acids, wherein said sample comprises a labeled positive control target nucleic acid;

(b) contacting said labeled sample under [stringent] hybridization conditions that require a target nucleic acid of 14 nucleotides in length to have at least 70% sequence identity with a probe in order to hybridize to said probe with a collection of substrate bound features comprising:

(i) test-background features that may or may not selectively hybridize to said target nucleic acids that include a positive control probe, and

(ii) standard-background features that are known to not selectively hybridize to said target nucleic acids

wherein said substrate bound features are present on said substrate in a spatially defined and a physically addressable manner;

(c) removing unhybridized target nucleic acids from said substrate;

(d) determining a test-background signal by detecting a signal for each test-background feature and averaging said test-background feature signals;

(e) determining a standard-background signal by detecting a signal for each standard-background feature and averaging said standard-background feature signals;

(f) comparing the amount of the test-background signal with the amount of the standard-background signal.

34. (Amended) A kit for use in the method of claim 10, said kit comprising:

an array having a plurality of background features, wherein said background features

comprise probes selected from the group consisting of empirically observed inactive probes, probes forming [stable] intramolecular structures, short probes of from 5 to 25 nt in length, reverse polarity nucleotide analogs, abasic phosphodiesters or modified nucleotidic units.

40. (Amended) A hybridization assay, said assay comprising:

(a) providing a sample of target nucleic acids that includes a positive control target nucleic acid;

(b) contacting said sample under [stringent] hybridization conditions that require a target nucleic acid of 14 nucleotides in length to have at least 70% sequence identity with a probe in order to hybridize to said probe with a collection of substrate bound nucleic acid features comprising:

(i) hybridization probes that include a positive control probe, and

(ii) background features

wherein said substrate bound nucleic acid features are present on said substrate in a spatially defined and a physically addressable manner;

(c) removing unhybridized target nucleic acids from said substrate;

(d) detecting an observed signal for at least one resultant detectable hybridization probe feature of said substrate;

(e) detecting a background feature signal for each resultant detectable background feature and determining a background signal from at least one of said detected background feature signals; and

(f) subtracting the background signal from the observed signal for each hybridization probe feature.

43. (Amended) The assay of claim 40, wherein the background features comprise probes selected from the group consisting of empirically observed inactive probes, probes forming [stable] intramolecular structures, short probes of from 5 to 25 nt in length, reverse polarity nucleotide analogs, abasic phosphodiesters or modified nucleotidic units.

44. (Amended) A hybridization assay, said assay comprising:

(a) providing a sample of labeled target nucleic acids that includes a positive control target nucleic acid;

(b) contacting said sample under [stringent] hybridization conditions that require a target nucleic acid of 14 nucleotides in length to have at least 70% sequence identity with a probe in order to hybridize to said probe with a collection of substrate bound nucleic acid features comprising:

(i) hybridization probes that include a positive control probe, and

(ii) background features

wherein said substrate bound nucleic acid features are present on said substrate in a spatially defined and a physically addressable manner;

(c) removing unhybridized target nucleic acids from said substrate;

(d) detecting an observed signal for each resultant detectable hybridization probe feature of said substrate;

(e) detecting a background feature signal for each resultant detectable background feature and determining a background signal from said detected background feature signals; and

(f) subtracting the background signal from the observed signal for each hybridization probe feature.

49. (Amended) The assay of claim 44, wherein the background features comprise probes selected from the group consisting of empirically observed inactive probes, probes forming [stable] intramolecular structures, short probes of from 5 to 25 nt in length, reverse polarity nucleotide analogs, abasic phosphodiesters or modified nucleotidic units.

REMARKS

Claims 10 to 32 and 34 to 49 are pending in this application.

Claims 10, 21, 30, 40 and 44 have first been amended to specify that the collection of target nucleic acids includes a positive control target nucleic acid, support for this amendment being found in the specification at page 15, line 27 ff as specifically exemplified in Example 1.

Claims 10, 21, 30, 40 and 44 have also been amended to remove the word stringent and insert specific hybridization conditions, support for the amendatory language being found in the specification at page 27, lines 18 to 22. Claims 10, 21, 30, 40 and 44 have also been amended to specify that the substrate includes a control probe, support for this amendment being found at page 15, line 27 ff as specifically exemplified in Example 1. Claims 10, 21, 30, 40 and 44 have also been amended to clarify that the features are present on the substrate in a spatially defined and physically addressable manner, support for this amendment being found in the specification at page 17, lines 28 ff. Claims 15, 24, 34, 43 and 49 have been amended to remove the word stable. These claims have also been amended to specify that the short probes are from 5 to 25 nt in length, support for this amendment being found in the specification at page 22, line 23 which specifically refers to table 5 that shows representative short probes ranging from 5 to 25 nt in length. As the above amendments introduce no new matter to the application, their entry by the Examiner is respectfully requested.

With respect to items 1 and 2 of the final rejection, it is respectfully submitted that the referenced Sambrook et al. manual is not relied on to provide meaning to any of the terms appearing in the claims and therefore need not be introduced into the specification as indicated by the Examiner.

Claims 10-32 and 34 to 49 have been rejected under 35 U.S.C. § 112, 1st ¶ for the asserted reason that the phrase "stringent hybridization conditions" introduces new matter to the application. While this phrase is specifically found in the specification at page 27, line 23, and therefore does not introduce new matter to the application, in view of the removal of this phrase from the claims, this rejection is rendered moot and may be withdrawn.

Claims 10-32 and 34 to 49 have been rejected under 35 U.S.C. § 112, 1st ¶ for the reasons asserted in the prior office action. In maintaining this rejection the Examiner provides no specific reasoning as to why the Applicant's earlier arguments were not persuasive, beyond a general discussion of what the law requires in terms of enablement. As such, no clarification was provided by the Examiner as to which of the four original specific reasons for this rejection were not addressed in the applicants prior response.

In making the prior rejection, the Examiner first asserted that claim 10 required one of skill in the art to definitively label a target nucleic acid sequence when the skilled artisan is not

even sure that such a sequence exists. In addition, the Examiner objected that there is no method step for achieving said labeling.

In response, the Applicant amended claim 10 to clarify the labeling of the target nucleic acid. It is noted that the specification provides an exhaustive description and review of different nucleic acid labeling protocols and therefore it is submitted that it would not require undue experimentation on the part of one skilled in the art to practice this step of the claimed methods.

Further, the amendment specified that the entire sample of target nucleic acids is labeled. As such, there was no requirement in the claimed method for one of skill in the art to label a nucleic acid that may not even be present. In order to further address this point, the claims have been amended to specify that the target nucleic acids include a positive control, which the practitioner will know is present in the mixture.

As such, it is believed that this first original reason for the rejection has been addressed and is no longer an issue.

Second, the Examiner asserted that claim 10 did not recite any means by which the skilled artisan is to be able to discriminate between, and independently measure, the signal from the target sequence and the background signal. In addition, claims 11-20, which depend on claim 10, were asserted to not enable one skilled in the art to make such measurements.

In response, the Applicant amended claim 10 to clarify that the nucleic acid features are bound to a substrate. A further modification has been made to the claims in this response to specify that the features are bound to the substrate in a spatially defined and physically addressable manner. As such, when read in light of the specification, the skilled artisan would see that such binding is done with knowledge as to the location of each feature. Thus, one skilled in the art would know the location of both the hybridized labeled target sequence and the background features. The skilled artisan could then independently and discriminately measure both the observed signal and the background signal using the methods set forth in the instant

invention.

As such, it is believed that this second original reason for the rejection has been addressed and is no longer an issue.

Third, the Examiner objected that the claimed method did not recite any conditions under which the hybridization reaction is to take place. Further, the Examiner asserts that neither the claims nor the specification set forth in sufficient detail an enabling disclosure whereby one of skill in the art would be able to perform the claimed assay without having to take such issues into consideration. As now amended, specific hybridization conditions that are fully supported by the specification and readily determinable without undue experimentation by one of skill in the art are now present in the claims.

As such, it is believed that this third original reason for the rejection has been addressed and is no longer an issue.

Fourth, the Examiner contended that claims 21-29 were not adequately enabled by the disclosure because they did not recite adequate method steps to allow one of skill in the art to estimate background noise.

In response, the Applicant amended claim 21 to clarify the steps required to arrive at an estimate of the background noise. Thus, one skilled in the art would be able to use the methods of the claimed invention to estimate background noise.

As such, it is believed that this fourth original reason for the rejection has been addressed and is no longer an issue.

Therefore, as now presented the Applicant has enabled the claimed invention and respectfully requests that this rejection of claims 10 to 32 and 34 to 49 under 35 U.S.C. §112, first paragraph, be withdrawn.

Claims 10-32 and 34-49 were rejected under 35 U.S.C. § 112, 2nd ¶ for the asserted reason that the phrases: (1) stringent hybridization conditions; (2) short probes; and (3) stable; are indefinite. In view of the removal of the phrase "stringent hybridization conditions" from the claims; the clarification in the claims that short probes range in length from 5 to 25 nt and the removal of the word "stable" from the claims; it is respectfully submitted that this rejection may be withdrawn.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815.

Respectfully submitted,

Date: 2·9·01

By: _____
Bret E. Field
Registration No. 37,620

Amendment after final